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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,400	02/20/2002	Harry Meade	10275-041002	3033

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EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	**PAPER NUMBER**
1632	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/081,400	MEADE ET AL.	
	Examiner	Art Unit	
	Joseph T. Woitach	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 February 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26, 45-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *48-67* is/are allowed.

6)☒ Claim(s) *1-26,46,47 and 68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *27 January 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This application filed February 20, 2002, is a divisional of 09/333,213 filed June 15, 1999, now US Patent 6,548,653, which claims benefit to 60/089,343 filed June 15, 1998.

Applicants' amendment filed February 25, 2005, has been received and entered. The specification has been amended. Claims 27-45 have been canceled. Claims 1, 2, 18, 19, 23, 24, 26, 46 and 47 have been amended. Claims 48-68 have been added.

Claims 1-26, 46-68 are pending.

Election/Restriction

Applicants elected group I, drawn to a erythropoietin serum albumin fusion protein without traverse. Newly added claims 48-68 are drawn to the elected invention. Claims 1-26, 46-68 are pending and currently under examination.

Specification

The nucleotide sequence disclosure contained in this application complies with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825.

Applicants filing of the sequence listing and other supporting materials have addressed the requirements of 37 C.F.R. 1.821 - 1.825. Further, it is noted that the specification has been amended to identify each of the listed sequences throughout the entire specification.

Drawings

The corrected drawings filed January 27, 2005 have addressed the issues raised in the previous action. Specifically, the amendment includes the SEQ ID NO for sequences set forth in the drawing.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-26, 46 and 47 stand and newly added claims 48-68 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 56-81, 88-101, 106-111 of copending Application No. 10/768,873

Applicants note the rejection is a provisional rejection, and note that upon allowance if appropriate, a terminal disclaimer would be filed. Applicants comments are noted, however since each application is still pending neither have claims in condition for allowance, the rejection is maintained.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims encompass the same EPO-SA fusion protein with methods of making and using that have only one obvious use in making said fusion proteins.

Again, this is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC ∋ 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-26, 46 and 47 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn.

The amendments to the claims to more clearly set forth that the EPO is a obtained from human has obviated the basis of the rejection.

Newly added claim 68 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the claim sets forth a composition that has an therapeutically effective amount of an EPO-SA fusion protein, however a therapeutic amount can only be determined by the intended use and would be relative to any particular use. The metes and bounds are indefinite because they are related to a relative use.

Claim Rejections - 35 USC 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-26, 46 and 47 stand rejected and newly added claim 68 is rejected under 35 U.S.C. 103(a) as being unpatentable over Bill *et al.* (BBA, 1995), Bill *et al.* (BBA, 1997), Korhonen *et al.* (European Journal of Biochemistry 245:482-489, April, 1997), and Syed *et al.* (all references listed in IDS).

Applicants summarize the requirements for making a proper rejection under 35 USC 103, citing MPEP 2141 and the appropriate case law (pages 4-5 and page 7). Summarizing the teachings of each of the cited references, Applicants argue that combination of references fail to provide adequate motivation or expectation of success of the instantly claimed invention (page 5). Reviewing each of the references Applicants note how elements of each vary from the now amended claimed invention, in particular that some of the fusion proteins are designed for cleavage which is not the intent of the claimed fusion protein (Bill) and that the claimed fusion

protein would have a different pharmokinetics, glycsylation and steric activity than that of the combined references (Syed and Korhonen) (pages 5-7). See Applicants' amendment, pages 4-7. Applicants' arguments have been fully considered, but not found persuasive.

Initially, where Applicants are arguing that the cited references do not expressly suggest the claimed invention it is noted that case law supports that a reference must be considered not only for what it expressly teaches, but also for what it fairly suggests. *In re Burkel*, 201 USPQ 67 (CCPA 1979). Furthermore, in the determination of obviousness, the state of the art as well as the level of skill of those in the art are important factors to be considered. Further, the test for combining references is not what the individual references themselves suggest, but rather what the combination of disclosures taken as a whole would have suggested to one of ordinary skill in the art. *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Thus, for the purpose of combining references, those references need not explicitly suggest combining teachings, much less specific references. *In re Nilssen*, 7 USPQ2d 1500 (Fed. Cir. 1988). In this case, that art of record teaches that modified forms of EPO which were altered to affect the glycosylation of EPO, and in the form of a fusion protein were known and reduced to practice. Further, the pharmokinetic affects of fusing SA to a protein to form a fusion protein were also known. Both Bill *et al.* and Korhonen *et al.* teach methods of making an EPOa fusion proteins. Syed *et al.* teach that fusion proteins containing serum albumin are more stable and cleared more slowly if administered to a subject. Combined with the teachings of Bill *et al.* of the nucleic acid sequences that encode human EPO, Syed *et al.* provide the necessary guidance to successfully generate the vectors and methodology to produce the fusion protein in mammalian cells. Thus all of the elements encompassed by the claims are taught by the cited references.

Examiner agrees that none of the references explicitly set forth the claimed invention, however it was scientifically reasoned in the basis of the rejection that in light of the knowledge in the art and the specific teachings of Bill *et al.* or Korhonen *et al.* that EPO is a secreted protein found in the circulation and that other forms of EPO are presently used in clinical applications, one would be motivated to use the teachings of Syed *et al.* in order to produce a fusion protein which is cleared more slowly than EPOa alone from the circulation. It is maintained that it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the isolated nucleic acid encoding EPOa and the methods of Bill *et al.* and the expression constructs and methods of Syed *et al.* to produce an EPOa-hSA fusion protein.

Applicants argue that the claimed invention would have properties different from that of the combined references. This is not found persuasive because there is no evidence to this fact. It is noted that the arguments of counsel cannot take the place of evidence in the record . *In re Schulze*, 346 F.2d 600, 602, 145 USPQ 716,718 (CCPA 1965). Examples of attorney statements which are not evidence and which must be supported by an appropriate affidavit or declaration include statements regarding unexpected results. MPEP 716.01(c). In addition, in this case the claims are very broad, and it is noted that the claims do not even require an active form of EPOa, nor an activity or any other pharmokinetic properties. Even if a particular form of a fusion protein were made and demonstrated to have a particular property, there is the general expectation that the fusion with SA would increase the half-life of any protein, and with EPO would thereby increase the affect of EPO in a subject.

Given the state of the art at the time the invention was made, there would have been a reasonable expectation of success to substitute EPOa described by Bill *et al.* or Korhonen *et al.*

for hirudin to create an expression construct and express an EPOa-serum albumin fusion protein with the methods described by Syed *et al.* Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). Further, it was noted previously that there does not appear to be any limitation to making other fusion EPO and SA proteins by simply substituting the nucleic acid encoding SA into the vector described by Bill *et al.* for expression in *E. coli* and generating an EPO-SA fusion protein.

Newly amended claims 1-26, 46 set forth that the EPO sequence is human and the modified form is derived therefrom. Bill *et al.* teach nucleic acid sequences that encode human EPO. Newly added claim 68 indicates that the composition of claim 50 is a pharmaceutical composition. Even in light of the issues raised under 35 USC 112, second paragraph, a pharmaceutical can be reasonably interpreted to any composition that can be delivered to a subject. In light of the teaching of the cited references that SA increases the life of a fusion protein in the circulation of a subject, the claimed invention as a whole was clearly *prima facie* obvious.

Therefore, for the reasons above and of record, the rejection is maintained.

Conclusion

Claims 48-67 are allowed. Claims 48-67 are free of the art of record because while there is teaching and motivation to alter the various glycosylation sites in human EPO, there is no motivation to change each of the glycosylation sites, in particular because the art teaches that even single alterations can result an EPO protein with less activity than the non-modified form.

While the art of record provides teachings and evidence that simple modifications to EPO can be made that result in a functional protein, the art of record fails to provide adequate motivation nor the expectation that one can successfully alter all the glycosylation sites of EPO. Further, while SA is added to provide greater stability when the fusion protein is present in the circulation of a subject, there would be no motivation to link an inactive form of EPO protein to SA for any purpose.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (571) 272-0739.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla, can be reached at (571) 272-0735.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (571) 272-0532.

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